

Claims 5, 6, 10-17, 19 and 20 have been canceled. Claims 1-4, 7-9, 18 and newly presented claims 21-23 are still at issue and are present for examination.

Applicants' arguments filed on 3/2/08, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim 18 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/16/06.

Claims 22 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 and 23 recite that the "first propeptide is complement C1q-C subunit C-terminus". However this is indefinite as to what portion of the complement C1q-C subunit beyond just the C-terminal residue must be present. Does this include any fragment of the complement C1q-C subunit comprising the C-terminal residue, or only fragments which include some

particular portion of the complement Clq-C subunit (such as that described by the method of Example 2F)

Claims 1-4, 7-9, and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant procollagen comprising a natural collagen polypeptide chain, a natural C-terminal collagen propeptide, and a first non-natural site-specific proteolytic agent recognition site, wherein said first non-natural site-specific proteolytic agent recognition site is located between said collagen chain and said natural C-terminal collagen propeptide, and further comprising an amino terminal propeptide and a second non-natural site-specific proteolytic agent recognition site, wherein said second non-natural site-specific proteolytic agent recognition site is located between said N-terminal propeptide and said collagen chain, does not reasonably provide enablement for a recombinant procollagen comprising a natural collagen polypeptide chain and any C-terminal propeptide, and a first non-natural site-specific proteolytic agent recognition site, wherein said first non-natural site-specific proteolytic agent recognition site is located between said collagen chain and said C-terminal propeptide, and further comprising an N-terminal propeptide and a second non-natural site-specific proteolytic agent recognition

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site, wherein said second non-natural site-specific proteolytic agent recognition site is located between said collagen chain and said amino terminal propeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is explained in the previous Office Action.

Applicants traverse the rejection by arguing that the claims do not recite or require any disulfide bond or triple helix formations and thus presumably that it is irrelevant whether the procollagen molecule can be glycosylated and correctly form disulfide bonds and a triple helix with other collagen chains. However, it is not irrelevant whether the claimed procollagen chains can be glycosylated and correctly form disulfide bonds and a triple helix with other collagen chains as without these abilities they cannot be used as known in the art. Applicants are required to teach how to use the full scope of the claimed molecules. The use of the claimed procollagens asserted by the specification is for the production of biologically active collagens. However procollagen chains which have different C-terminal propeptides (or no C-terminal propeptide as would be produced by cleavage of the non-natural C-terminal propeptide at the non-natural site-specific

proteolytic agent recognition site of the construct) would not be useful for producing a biologically active collagen as they are not correctly processed. As such the specification fails to teach how to use the full scope of the claimed invention.

Applicants further state in the response "We also note that the proposal goes beyond any support in the cited references, and is not technically correct; see, e.g. Zhang et al., J. Biol. Chem., Vol. 276, Issue 23, 19862-19870, June 8, 2001 (attached), esp. Fig. 8 and related discussion". However, this statement is completely incomprehensible as applicants do not explain what they think is not technically correct nor how they are relying on Zhang et al. to traverse the instant rejection. If applicants are trying to indicate that Fig 8 of Zhang et al. shows a construct in which a heterologous C-terminal propeptide was added to a natural collagen polypeptide chain and successfully formed a triple-helix, it is noted that the specific C-terminal propeptide of Zhang et al. is in fact a peptide region of a different protein which has activity within that protein of providing for trimerization and triple-helix formation. As such this reference might evidence that heterologous C-terminal peptides with trimerization and triple-helix formation activity would be suitable in addition to the natural procollagen C-terminal propeptide. However, this is not

a functional requirement of applicants claims, the instant specification provides no indication, that C-terminal propeptides having this activity should be used and the teaching of Zhang et al. is post-filing and thus can not be used to provide the necessary guidance to one of skill in the art for selecting suitable heterologous C-terminal propeptides. As such the rejection is maintained.

With regard to new claims 21 and 23 which recite ubiquitin as the heterologous C-terminal propeptide, these claims are also not enabled despite Examples 2 F and G as these example merely describe how to make constructs with this heterologous C-terminal propeptide and do not in any way show the successful use of any such procollagen chain. It is noted that the portion of the examples which describe production of a recombinant collagen molecule from said procollagens and use thereof are merely prophetic without any actual showing of successful use of a procollagen chain produced as described in Examples 2 F and G. As such use of these procollagens is also not enabled by the specification.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this

action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached at (571) 272-0934. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
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